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RESEARCH ARTICLE

Correlation of bleeding time and clotting time in different phases of menstrual cycle

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ABSTRACT

Background: Changes in the levels of female sex hormones during the menstrual cycle are known to affect the coagulation cascade by producing parallel changes in the prothrombotic tendency and the fibrinolytic activity of healthy women. **Aims and Objectives:** The aims of the study was to access the changes in bleeding time (BT) and clotting time (CT) during different phases of menstruation. **Materials and Methods:** Study was conducted in the Department of Physiology, TMMC and RC over a period of 1 year. A group of 40 females between the age group of 18–25 years having normal menstrual cycle were selected. Females with hormonal disorders, taking hormonal medication having hematological, gynecological or any chronic disorder were excluded. There BT and CT were accessed in four phases of menstrual cycle, i.e., menstrual phase, proliferative phase, ovulatory phase, and secretory phase. Data were analyzed using SPSS software. **Results:** The mean BT shows a significant difference ($P = 0.001$). BT was least around the Ovulatory Phase or mid-cycle, and it increases during secretory phase. CT was least around ovulatory or mid-cycle, and it increases during secretory phase. However, the difference of CT in different phases was not statistically significant. **Conclusion:** The present study indicates that primary and secondary hemostatic mechanism activities are higher in the follicular and ovulatory phase than remaining phases. Hence, optimal hemostatic testing time must be done in menstrual and early follicular phase.

KEY WORDS: Bleeding Time; Clotting Time; Menstrual Phase; Ovulatory Phase; Proliferative Phase; Secretory Phase

INTRODUCTION

Menstruation is defined as monthly women's cycle which is the unique, distinctive attribute of femininity. The term menstruation and menses were derived from the Latin word; it means month.[1] Menstruation cycle is comprehended of two cycles, namely ovarian cycle and uterine cycle based on occurrences in the ovary and the uterus, respectively.[2] The ovarian cycle comprised three phases of follicular phase, ovulation, and luteal phase. Menstrual, proliferative, ovulatory and secretory phases are come under uterine cycle. The endocrine system is fully governs both cycles. Conventionally, 1st day of bleeding is considered to be the 1st day of the endometrial cycle. The endometrial cycle of 28 days can be divided into four phases - menstrual phases (1–5th day), proliferative phase (6–13th day), ovulatory phase (14th day), and secretory phases (15–28th day). Several reports have been confirmed that the bleeding and clotting system is dependent on the hormonal changes during menstrual cycle.[3]

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Bleeding time (BT) is time from prick till stoppage of bleeding. It lasts for 3–4 min.[4] Clotting time (CT) is the time period from the inception of bleeding to first fibrin thread formation. Normal value of CT is 5–8 min.[5]

The most common hereditary bleeding disorder is Von-Willebrand disease, menorrhagia or heavy menstrual bleeding occurs in the majority of women with bleeding

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disorders. The American College of Obstetrics and Gynecology has recommended that women with heavy menstrual bleeding should have diagnostic testing for bleeding disorders.[6] The major focus of the present investigation is to demonstrate the BT and CT variations during the menstrual cycle.

MATERIALS AND METHODS

The study was carried out in the Hematology Laboratory of Department of Physiology, Teerthanker Mahaveer Medical College and Research Centre, Moradabad (U.P), over a period of 12 months after approval from the college Ethical committee.

Inclusion Criteria

The following criteria were included in this study:
- Females of the age 18–25 years,
- Who had given written informed consent,
- Having regular menstrual cycle (a normal menstrual cycle was taken as a cycle from 21 to 35 days which are past for 2–6 days).

Exclusion Criteria

The following criteria were excluded from the study:
- Females with hormonal disorders[7]
- Taking hormonal medications[7]
- Alcohol consumption and smoking[7]
- Hematological disorders[8]
- Systemic, chronic, or gynecological disease[9]
- Chronic drug user (nonsteroidal anti-inflammatory drugs)[10] contraceptive pills[11]
- Recent history of viral infections such as dengue and hepatitis[12]

BT and CT were assessed under the following phases of menstrual cycle:
1. Menstrual phase (2nd day)
2. Proliferative phase (9th day after 1st sample)
3. Ovulatory phase (14th day after 2nd sample)
4. Secretory phase (8 days after 3rd sample).

The BT was estimated by Duke's method using Whatman filter paper[13] CT was estimated by capillary tube method.[13]

Statistical Analysis

The data were collected, tabulated and were analyzed using SPSS (version 23). Comparison between the mean of BT and CT in all phases of menstrual cycle was done by Friedman's test. The intergroup comparison of BT and CT in menstrual cycle phases was done by Wilcoxon sign-ranks test. $P < 0.05$ was considered statistically significant.

RESULTS

A total of 40 females were included in the study. Mean BT (sec) was compared between the phases of the menstrual cycle using the Friedman's test. The mean BT shows a significant difference ($P = 0.001$). BT was least around the Ovulatory Phase or mid-cycle, and it increases during secretory phase [Table 1].

In Table 2, the intergroup comparison of mean BT (sec) was done using the Wilcoxon sign-ranks test. Significant difference was found for the intergroup comparison of mean BT between the phases of menstrual cycle.

In Table 3, the mean CT (sec) was compared between all the phases of the menstrual cycle using the Friedman's test. CT was at least around ovulatory or mid-cycle, and it increases

Table 1: Comparison of BT between menstrual phase, proliferative phase, ovulatory phase, and secretory phase (n=40)

Phases	BT (sec)		
	Mean±SD	Critical value	*P* value
Menstrual phase	117.00±25.24	31.213	0.001*
Proliferative phase	116.25±32.00		
Ovulatory phase	99.88±16.27		
Secretory phase	123.75±22.95		

*P<0.05 (significance); >0.05 (not significance). BT: Bleeding time

Table 2: The intergroup comparison of mean BT between menstrual phase, proliferative phase, ovulatory phase, and secretory phase (n=40)

Phases		Mean difference	*P* value
Menstrual phase	Proliferative phase	0.75	0.793
Menstrual phase	Ovulatory phase	17.13	0.001*
Menstrual phase	Secretory phase	−6.75	0.150
Proliferative phase	Ovulatory phase	16.38	0.001*
Proliferative phase	Secretory phase	−7.50	0.107
Ovulatory phase	Secretory phase	−23.88	<0.001*

*P<0.05 (significance); >0.05 (not significance). BT: Bleeding time

Table 3: Comparison of mean CT between menstrual phase, proliferative phase, ovulatory phase, and secretory phase (n=40)

Phases	CT (sec)		
	Mean±SD	Critical value	*P* value
Menstrual phase	195.00±58.83	2.648	0.449
Proliferative phase	189.00±60.84		
Ovulatory phase	180.25±44.40		
Secretory phase	190.00±59.53		

P<0.05 (significance); >0.05 (not significance). CT: Clotting time

during secretory phase. However, the difference of CT in various phases was not statistically significant.

In Table 4, the intergroup comparison of mean CT (sec) was done using the Wilcoxon sign-ranks test. No significant difference was found for the intergroup comparison of mean CT between the phases of menstrual cycle.

DISCUSSION

The mean BT of menstrual phase, proliferative phase, ovulatory phase, and secretory phase was 117.00, 116.25, 99.88, and 123.75, respectively. There was a significant difference (P = 0.001) in mean BT between menstrual phase, proliferative phase, ovulatory phase or mid-cycle, and secretory phase. BT was at least around the mid-cycle, and it increases during secretory phase. The intergroup comparison of mean BT between menstrual cycle phases shows a statistically significant change. The mean CT in menstrual phase, proliferative phase, ovulatory phase, and secretory phase was 195.00, 189.00, 180.25, and 190.00, respectively. There was no significant difference (P = 0.449) in mean CT between all the phases of menstrual cycle. CT was found to be lowest at the mid-cycle, and it gradually increases in the secretory phase. Statistical significant variation of mean CT was not showed in all the phases of menstrual cycle.

Sulaxane *et al.* studied the changes in BT and CT in various phases of menstrual cycle. Height, weight, body mass index, blood pressure, pulse, BT, and CT were recorded in 60 healthy females. It was observed that BT at follicular phase was significantly lower than menstrual and luteal phases. Among all the phases of menstrual cycle, follicular phase showed lowest mean of CT, but not statistically significant.[14] Indirect evidence suggested that hormonal fluctuation during the menstrual cycle also affect the bleeding and clotting system.[15] Changes in the levels of female sex hormones during menstrual cycle are known to affect the coagulation cascade by producing parallel changes in the prothrombotic tendency and the fibrinolytic activity of healthy women. There is variation in the number of platelets and platelet retention during different phases of menstrual cycle.[16] Balasubramaniam *et al.* concluded that increase of platelet count could be the valid reason for shortening the BT during the mid-cycle.[17] We found that mean BT at Ovulatory phase or mid-cycle was significantly ($P < 0.001$) lower in comparison to other phases of menstrual cycle. It could be the combined effect of higher availability of platelets and aggregation around the pre-ovulatory peak of estrogen. The initial 4 days of menses appeared to have lower platelet count and started gaining the platelet count afterward. However, platelet count may be raised by 1.4 lakhs/mm^3 in blood at the time of ovulation.[18] Rajnee *et al.* studied the effect of menstrual cycle on hematological parameters among 30 healthy female in the age group of 18–23 years. The CT was taken on the 2nd, 11th, 14th, and 22nd day of menstrual cycle. It was concluded that CT not significantly varies during all the phases of menstrual cycle. CT was at least around the mid-cycle, and it increases during secretory phase.[6] Angel *et al.* studied the variation in bleeding and CTs during menstrual cycle on forty healthy female (mean age 21 ± 2) there was no significant variation in CT observed during all the phases of menstrual cycle.[19] Our study supports earlier studies as we have also observed the mean BT shows a significant difference in different phases of menstrual cycle. It is least around the ovulatory phase or mid-cycle and it increases during secretory phase. Moreover, there was no significant difference in mean CT between all the phases of menstrual cycle though it was found to be lowest at the mid-cycle and it gradually increases in the secretory phase.

We need to extend this study to a bigger group. The future studies can be conducted using advanced test methods including platelet aggregation studies, prothrombin time, activated partial thromboplastin time, platelet function analyzer closure time, and coagulation factor.

The present study indicates that primary and secondary hemostatic mechanism activities are higher in the follicular and ovulatory phase than remaining phases. However, optimal hemostatic testing time must be done in menstrual and early follicular phase.

Table 4: The intergroup comparison of mean CT between menstrual phase, proliferative phase, ovulatory phase, and secretory phase (n=40)

Phases		Mean difference	P value
Menstrual phase	Proliferative phase	6.00	0.728
Menstrual phase	Ovulatory phase	14.75	0.295
Menstrual phase	Secretory phase	5.00	0.534
Proliferative phase	Ovulatory phase	8.75	0.194
Proliferative phase	Secretory phase	−1.00	0.934
Ovulatory phase	Secretory phase	−9.75	0.313

P<0.05 (significance); >0.05 (not significance). CT: Clotting time

CONCLUSION

There was a significant difference in mean BT between menstrual phase, proliferative phase, ovulatory phase or mid-cycle, and secretory phase. BT was at least around the mid-cycle, and it increases during secretory phase. The intergroup comparison of mean BT between menstrual cycle phases shows a statistically significant change. There was no significant difference in mean CT between all the phases of menstrual cycle. CT was found to be lowest at the mid-cycle, and it gradually increases in the secretory phase. The intergroup comparison of mean CT between different phases of the menstrual cycle is not statistically significant.

REFERENCES

1. Marilyn MS. Fertility Cycles and Nutrition: How Diet Affects Menstrual Cycles and Fertility. 3rd ed. Cincinnati, Ohio: Couple to Couple League Intl; 2008. p. 71-2.
2. Unglaub SD. Human Physiology: An Integrated Approach. 6th ed. Glenview, IL: Pearson Education Inc.; 2013. p. 850-90.
3. Brown D. Changes in Bleeding and Clotting During the Menstrual Cycle. Available from: https://www.ClinicalTrials.gov>NCT00480545. [Last accessed on 2018 Mar 15].
4. Bijlani RL, Manjunatha S. Understanding Medical Physiology. 4th ed. India: Jaypee Publication; 2010.
5. Guyton AC, Hall J. Text Book for Medical Physiology. 11th ed. Philadelphia, PA: Elsevier Saunders; 2005. p. 467.
6. Rajnee A, Chawla VK, Choudhary S, Binawara BK, Choudhary R. Haematological and electrocardiographic variations during menstrual cycle. Pak J Physiol 2010;6:18-2.
7. Pehlivanoglu B, Balkanchi ZD, Ridvanagaoglu AY, Durmazlar N, OzturkG, Erbas D, *et al.* Impact of stress, gender and menstrual cycle in immune system: Possible role of nitric oxide. Arch Physiol Biochem 2001;109:383-7.
8. Mohammed RS. The Ritual Ablutions for Women. Richmond, BC: Vancouver Islamic Education Foundation Publishers; 1985. Available from: http://www.al-islam.org/the-ritual-ablutions-for-women...muhammad-rizvi/intr. [Last accessed on 2018 Mar 15].
9. Widmaier EP, Hershel R, Strang KT. Vander's Human Physiology: The Mechanism of Body Function. 12th ed. New York, NY: Mc Graw Hill; 2010. p. 555-631.
10. Klump KL, Keel PK, Racine SE, Burt SA, Neale M, Sisk CL, *et al.* The interactive effects of estrogen and progesterone on changes in emotional eating across the menstrual cycle. J Abnorm Psychol 2013;122:131-7.
11. Schmidt PJ, Nieman LK, Danaceau MA, Adams LF, Rubinow DR. Differential behavioral effects of gonadal steroids in women with and in those without premenstrual syndrome. N Engl J Med 1998;338:209-16.
12. Guyton AC, Hall JE. Text Book for Medical Physiology. Philadelphia, PA: Elsevier Saunders, Second South Asia Edition; 2015. p. 664.
13. Khurana I. Textbook of Medical Physiology. London: Routledge; 2015. p. 852.
14. Sulaxane YD, Patel SG. Cyclic fluctuation of bleeding time and clotting time in various phases of menstrual cycle. Natl J Physiol Pharm Pharmacol 2015;5:328-32.
15. Danasu R, Rajalakshmi S, Christina AM. A study to asses relationship between body mass index (BMI) and menstrual irregularities among adolescent girls at selected nursing college, Pondicherry. Int J Inf Res Rev 2016;3:2725-29.
16. Begum J, Hossain AM, Nazneen SA. Menstrual pattern and common menstrual disorders among students in Dinajpur college. Dinajpur Med Col J 2009;2:37-43.
17. Balasubramaniam P, Parulkar VG, Bhatt JV. Some haematological observation during menstrual cycle. Indian J Med Sci 1980;3418:193-4.
18. Ganesh R, Ilona L, Fadil R. Relationship between body mass index with menstrual cycle in senior high school students. Althea Med J 2015;2:555-60.
19. Angel J, Sailesh KS, Divya, Jissa G, Mukkadan J.K. A study on variation of bleeding time and clotting time during menstrual cycle. Asian J Health Sci 2013;1:23-4.

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